REMARKS

Amendments to the Claims

Claims 1-5 and 9-17 were subject to examination. Claims 6-8 had been cancelled.

New Claims 18 and 19 are added.

New Claim 18 is based on Claim 1, and further provides that the transgenic mouse exhibits a behavioral phenotype that models a symptom of schizophrenia, and that the exhibited behavioral phenotype is selected from the behavioral phenotypes provided in Claim 4 as filed.

New Claim 19 depends from Claim 6 and further identifies and distinguishes the listed phenotypes as behavioral phenotypes and biochemical phenotypes.

No new matter has been added.

Claim Objections

Applicants first respectfully point out that the examination has been carried out on the set of claims as originally filed, and not on the current set of claims pending, which were presented in a preliminary amendment filed February 13, 2006. These are also the claims that published in US Application Publication 2008-0070237.

Consequently, the objection to the misnumbering of claims 6-8 is traversed as moot.

Claim Rejections

A. Claims 1-6 and 10-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Applicants traverse.

Applicants again respectfully point out that the rejection is asserted against the set of claims as originally filed, and not on the current set of claims pending, which were presented in a preliminary amendment filed February 13, 2006. Since at least Claim 1 was amended in the preliminary amendment, the rejection is *per se* as based upon the wrong set of claims.

Notwithstanding the error of the rejection, the current set of claims satisfies 35 USC 101.

Deficiencies under the "useful invention" requirement of 35 U.S.C. 101 will arise in one of two forms. The first is where it is not apparent why the invention is "useful." This can occur when an applicant fails to identify any specific and substantial utility for the invention or fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966); *In re Fisher*, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005);< *In re Ziegler*, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993). The second type of deficiency arises in the rare instance where an assertion of specific and substantial utility for the invention made by an applicant is not credible.

The law states that compliance with 35 U.S.C. 101 is met by providing a statement in the description of specific and substantial utility. The statement should fully and clearly explain why the applicants believe the invention is useful. Applicants' specification states at the beginning of paragraph [0065] that the claimed Npas3 knock-out mouse (Npas3-/-) is a model of schizophrenia. The specification also states in paragraph [0117] that potentially therapeutic agents for schizophrenia or related neurological disorders can be administered to Npas3-/- mice to evaluate and interpret their response or performance on specific behavioral tests or biochemical assays. Applicants therefore have identified a particular transgenic mouse (Npas3-/-) and have identified and demonstrated particular behavioral phenotypes of the mouse, and have explained how those behavioral phenotypes can be used to model the symptoms of a specific mental disorder, namely schizophrenia, and therefore Applicants' description does contain an assertion of specific and substantial utility for the invention, and therefore fully complies with 35 USC 101. Applicants note that the MPEP Guidelines cited by the Examiner references transgenic mice, but gives only the example of the transgenic mice as "snake food" as neither a specific (since all transgenic mice could function as snake food) nor substantial (using an expensive transgenic mouse as snake food is not a "real world" context use). Applicants' claimed invention describes a specific and substantial statement of utility, notwithstanding any doubt or alleged lack of credibility offered by the Examiner.

With all due respect to the Examiner's knowledge in this field of art, it is clear that the Applicants have disclosed enough information about the claimed invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. Applicants' description supports the statement of specific and substantial utility with the following:

1. the then-recent identification of schizophrenic patients with a deletion of the Npas3 gene (paragraphs [0011] and [0067]);

2. the showing that the neuroimaging of the brains of schizophrenic patients revealed characteristic abnormalities that also found in the brains of the Npas3-/- mice (paragraph [0080]); and

3. the demonstration that the Npas3-/- display the abnormal behavioral phenotypes associated with other mouse models of schizophrenia (beginning at paragraph [0081]), as compared to wild type.

The law also states that the applicant only needs to show a reasonable correlation between the asserted behavioral phenotype of the knockout mouse and the asserted utility. The Applicants are not required to show with certainty. *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA 1980). The applicant can establish this reasonable correlation by relying on statistically relevant data documenting the behavioral phenotypes of the claimed Npas3-/- mouse, arguments or reasoning, documentary evidence (e.g., Applicants' articles in scientific journals), or any combination thereof. The Applicant does not have to prove that a correlation exists between a particular behavioral phenotype and an asserted use of the Npas3-/- mouse for assessing therapeutic compounds for the treatment of schizophrenia as a matter of statistical certainty, nor do they have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the disclosed activity and the asserted use. *Nelson v. Bowler*, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

In most cases, Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. 101. See, e.g., *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (CCPA 1965); *In re Langer*, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (CCPA 1977). As the Court of Customs and Patent Appeals stated in *In re Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless

there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

If Applicants' asserted utility is credible (i.e., believable based on the record or the nature of the invention), a rejection based on "lack of utility" is not appropriate. An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. (MPEP 2107.02, III.B.)

Accordingly, the PTO must do more than merely question operability - it must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability. *In re Gaubert*, 524 F.2d 1222, 1224, 187 USPQ 664, 666 (CCPA 1975).

To establish that this burden has been met, the Action makes several general and unsupportable statements of fact about the Applicants' specification. The Examiner's statements in the Action on page 4, line 11, that "(a)t the time of filing, the skilled artisan would not have found such utilities evident because the specification only teaches general utilities that could apply to any knockout mouse. None of the utilities asserted in the instant specification are drawn to the disrupted Npas3 gene....", are grossly inaccurate and incredible. Applicants' description teaches that the Npas3-/- mouse displays several behavioral phenotypes that are clearly not generally applied to "any knockout mouse". The specification also teaches that the abnormal behavioral phenotypes displayed by the Npas3-/- mouse are not displayed in the wild type mouse, evidence that the asserted behavioral phenotypes are affected by the knockout of the Npas3 gene.

The Examiner continues to attack the credibility of the stated utility by going after the Npas3 gene. The Action continues on page 4 by also stating that "(t)he specification discloses no known function of the Npas3 gene". This is irrelevant. The Applicants are not claiming the Npas3 gene *per se* or its structure, but rather a transgenic mouse with a knockout of the Npas3 gene, and its use.

The Examiner continues on page 5, asserting that the usefulness of Applicants' Npas3-/- mice as models is not clear, "leaving the skilled artisan to speculate the uses of the transgenic

mouse, methods of use and cells of the claims". As previously established, the uses are expressly described by Applicants.

Continuing on page 5, the Examiner states "the use of the claimed mice to determine a function for the disrupted gene Npas3 lacks a specific or substantial utility as further research on the mouse is required to determine if the changes in behavioral phenotypes observed are associated with the loss of the specific gene product or due to the methodology used in making the mice." Again, the Examiner incorrectly identifies the invention as that of the Npas3 gene *per se*, and its utility. Applicants are not claiming the *Npas3* gene *per se*, but rather an Npas3 knockout mouse and its utility. These are quite different matters. Furthermore, none of the situations A. through E. discussed in the "utility guidelines" as requiring "further research" are applicable to the Applicants' claimed invention.

The question remains, is the Applicants assertion, that the Npas3-/- mouse has behavioral phenotypes that reasonably correlates with symptoms of schizophrenia, credible? That is, is it believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided by Applicants? Applicants believe so. Applicants' assertion is also credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. In this case, the Examiner must show that it is more likely than not that a person skilled in the art would not consider credible any specific and substantial utility asserted by the Applicants for the claimed invention. (MPEP 2107.02 IV.) The Examiner's statements of the facts and reasoning fall well short of meeting this burden of proof.

Finally, and curiously, the Action states on page 5 that "the increased insulin levels on mice comprising a disrupted Npas3 gene are not specific to any one disease or condition". Applicants do not know the relevance of this mention of "insulin" come from?

B. Claims 1-6 and 10-17 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants traverse.

Applicants again respectfully point out that the rejection was asserted against the set of claims as originally filed, and not on the current set of claims pending, which were presented in a

preliminary amendment filed February 13, 2006. Since at least Claim 1 was amended in the preliminary amendment, the rejection is *per se* as based upon the wrong set of claims.

Applicants request reconsideration of the rejection in view of the obvious difference between the present claims, and the claim set incorrectly considered by the Examiner. Applicants particularly emphasize that the claimed invention does not provide a schizophrenic mouse, as alleged by the Examiner, but rather provides a knockout mouse that has a phenotype (and particularly a behavioral phenotype) that models schizophrenia.

CONCLUSION

Applicants believe that a complete response to the outstanding action has been made, and that all claims should be found allowed.

Respectfully submitted,

For: E. W. BRUNSKILL et al.

By: _____

Daniel F. Nesbitt
Attorney for Applicants
Registration No. 33,746
(513) 229-0383
Customer Number 38155

May 27, 2009